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Original Article

The Use of Chitosan in the Preparation of Bioadhesive Buccal Films: Film-Forming Ability and Sustaining Ibuprofen Release

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Abstract

Aim: Different polymers were introduced into Chitosan bioadhesive buccal films to achieve substantial success in sustaining Ibuprofen release for few hours, with reasonable bioadhesion strength. **Design:** Thin, isolatable, transparent, and elastic films of these copolymers were prepared. Nineteen formulations have been classified as six systems according to the percentages of hydrocolloids used. **Materials and Methods:** The films were prepared using the solvent casting technique. Bioadhesion study was conducted using the stomach mucosa of a sacrificed albino rabbit. Hydrocolloids such as Hydroxy Propyl Cellulose (HPC), Chitosan, and Methyl Cellulose (MC), in addition to other polymers, were used in addition to Ibuprofen as a model drug. **Results:** The mechanical strength and flexibility of the films were confirmed with no signs of breaking down. Selected films composed of about 60% (w/w) HPC were found to show higher tendency to adhere to the stomach mucosa than lower percentages of the same polymer. Chitosan films have released more than 78% of Ibuprofen content in the 1st h of release study. The introduction of MC in these films has led to a slow but continuous increase in the percentage of drugs released, reaching the climax of 82% after 4 h. **Conclusion:** Films made of formulation (L17) were found to be the most ideal for both releasing appreciable amount of drug (about 98% in 4 h), and their high tendency to adhering to the rabbit mucosa (71.00 Mn/m) giving enough time to exert the drug's effect locally. The mechanism of drug release was found to follow Higuchi's diffusion model for some systems and the classical first-order kinetics for others.

Keywords: Bioadhesive films, cellulose derivatives, chitosan, ibuprofen, mechanism of drug release

Introduction

The use of chitosan as a film matrix former is well documented for the delivery of many hydrophilic and hydrophobic drugs to prolong the residence of a drug at the application site.[1] The matrix in these systems swells and forms a gel-like layer in an aqueous environment, by absorbing water from the mucous layer in the nasal cavity and buccal cavity, which favors the fluids interpenetration of polymer and glycoprotein chains into the mucous layer. A homogenous film matrix that contains the drug can be easily produced by dissolving Chitosan and the drug in the same vehicle.[2] The ability of Chitosan to form films explains its extensive use in the formulation of films in addition to other drug delivery systems.[3] Chitosan could be dissolved in organic acids, such as lactic acid and acetic acid, before being casted into films.[4] Chitosan films prepared by using acetic acid as a solvent represent effective controlled release systems for many water-soluble and insoluble drugs such as indomethacin,[5] tetracycline,[6] and propranolol hydrochloride.[7]

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The main advantages of the polymeric films are the possibility of programmed drug delivery by controlling the macromolecular structure and chemical nature of the polymeric matrix at the same time reducing the toxic side effects and the frequency of administering of commonly used drug dosage forms.[8] Chitosan films and hydrogels of chlorhexidine gluconate were studied specifically to prolong the residence time of drugs in the oral cavity.[1] Furthermore, many investigators have utilized Chitosan as a coating agent for liposome formulations with particle sizes below 1 μm, thereby creating hybrid systems frequently termed as Chitosan films. The amino groups that carry positive charges on the Chitosan molecules interact with

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negative charges on liposomes, viruses, proteins, and bacteria to form coating films around them.[9] *In vitro* release studies where based on the Noyes-Whitney equation[10] which predicts that the dissolution rate is a function of concentration gradient according to the equation:

$$Dc/Dt = K (Cs - C) \quad \text{Equation 1}$$

Where Dc/Dt = Dissolution rate of the drug, Cs = Concentration of the saturated solution, C = Concentration in the bulk solution, and k = Rate constant.

The main objective of this project is to prepare and evaluate bioadhesive buccal films made of Chitosan alone and Chitosan combined with other polymers namely: Sodium alginate, poly-vinyl-pyrelidone (PVP), methylcellulose (MC), ethyl cellulose (EC), hydroxyl EC (HEC) and hydroxyl propyle cellulose (HPC) as a release retarding system loaded with Ibuprofen as a model for poorly water-soluble drug using 1% lactic acid as a vehicle for the solubilization of Chitosan. Another objective of this work is to investigate the possible mechanism by which the drug is released from these systems.

Materials and Methods

Materials

Polymers used were chitosan from shrimp shells 75% deacetylation (Sigma Aldrich, Iceland), EC viscosity of 100 cp in (Sigma-Aldrich, USA), MC viscosity of 4000 cp in (Sigma-Aldrich, USA), polyvinylpyrrolidone (Merck, Darmastadt, Germany), hdroxypropylcellulose average MW100,000 (Hass, Ctradinghouse, Bellgium), sodium alginate (BDH Chemicals ltd Poole England). Model drugs including ibuprofen MW: 206.28 (Sigma-Aldrich, China), lactic acid (BDH chemicals ltd Poole England), acetic acid (GPR, limited Poole England), ethanol 99.6% (Riedel-de Haen), methanol (Sigma-Aldrich, Iceland), sodium hydroxide pellets (GRB, winiab laboratory chemical), potassium dihydrogen orthophosphate (BDH chemicals ltd, England), lactose (E. Merck, Darmstadt, Germany).

Equipment

Balances used was Sartorius bp121s and Sartorius bl600 (Canada), USP dissolution apparatus (Pharmatest dt70, Germany), ultraviolet visible spectrophptometer (Jenway 6305, Germany), pH meter (Handy-lab, Schott glaswerke, Mainz, Germany), force tensiometer (kruss GMBH, model k6, Germany), digital micrometer (Mitutoyo Digimatic type 40 EWS, Japan).

Methodology

Preparation of chitosan films using 1% lactic acid

Accurately weighed quantity of Chitosan was dissolved in accurately measured volume of 1% lactic acid and the required quantity of either sodium alginate, PVP, HEC, HPC, EC, or MC was dissolved in distilled water and then added to Chitosan solution with continues stirring to obtain the homogeneous solution of formulations from L1 to L19 (EC was dissolved in 20 ml ethanol), and the required amount of ibuprofen (20% w/w) was added to the formed solution and stirred for 15 min to disperse the drug in the polymeric solution. The films were cast by pouring 5 mls of each polymer solution in glass Petri dishes which were left in the hood allowing the solution to evaporate at room temperature. Each formulation was prepared in triplicate. Dry thin films were obtained after 24 h at room temperature and stored in dry place for further use. Formulations compositions are shown in Tables 1 and 2.

Table 1: Composition of formulations L1-L10 (% w/w)

Ingredient	L1	L2	L3	L4	L5	L6	L7	L8	L9	L10
Chitosan (%)	80	60	40	20	60	40	20	60	40	20
Na-Alginate (%)	-	20	40	60	-	-	-	-	-	-
PVP (%)	-	-	-	-	20	40	60	-	-	-
MC (%)	-	-	-	-	-	-	-	20	40	60
1% lactic acid (ml)	30	30	30	30	30	30	30	30	30	30
Distilled water (ml)	-	30	10	30	-	-	-	10	10	10
Ibuprofen (%)	20	20	20	20	20	20	20	20	20	20

PVP: Poly-vinyl-pyrelidone, MC: Methyl cellulose

Table 2: Composition of formulations L11-L19 (% w/w)

Ingredient	L11	L12	L13	L14*	L15*	L16*	L17	L18	L19
Chitosan* (%)	60	40	20	20	60	40	60	40	20
HEC (%)	20	40	60	-	-	-	-	-	-
EC (%)	-	-	-	60	40	60	-	-	
HPC (%)	-	-	-	-	-	-	20	40	20
1% lactic acid (ml)	30	30	30	20	20	20	30	30	30
Distilled water (ml)	10	10	10	5	5	5	10	10	10
Ibuprofen (%)	20	20	20	20	20	20	20	20	20

*Formulations L14-L16 contain 20 ml ethanol. EC: Ethyl cellulose, HEC: Hydroxyl EC, HPC: Hydroxy propyl cellulose

In vitro drug release

Drug release studies were conducted using United States Pharmacopea (USP) dissolution Apparatus-2 paddle type, at rotational speed of 50 rpm at 37°C ± 0.5°C. One side of the film was fixed to the bottom of a Petri dish using sieve wire (to prevent the film from floating upward). The dissolution media used were 350 ml of phosphate buffer solution (pH 7.4). Samples (5 ml each) were withdrawn at predetermined time intervals and replaced with the same volume of fresh dissolution medium to maintain the volume constant, therefore, maintaining the sink condition. The withdrawn samples were filtered through the 0.45-µm membrane filter. The drug content in each sample was determined spectrophotometrically at maximum absorbance wavelength 221 nm, after proper dilution. The release studies were performed in triplicate. The content of drug was driven from a standard Ibuprofen calibration curve of phosphate buffer pH 7.4.

Characterizations of the chitosan films

Determination of film thickness

Films of different thicknesses were prepared by film casting technique. Three formulations of different Chitosan to HPC ratios were prepared following the procedure described above. Five ml, 7 ml and 10 ml of each polymeric solution were poured into glass Petri dishes (diameter 4.6 cm). The dishes were left in the hood for evaporation of the solvent at room temperature leaving dry thin films after 24 h and then, the films were stored individually between sheets of wax paper and kept in a dry place. Three films of each formulation were isolated and the thicknesses of the films were measured using a digital micrometer probe. The instrument was calibrated using standard metal provided with the instrument. The readings were recorded at different points of the film surface and then the average film thicknesses were calculated.

Film surface pH study

The surface pH of the films was determined by allowing the film to swell in presence of 5 ml of distilled water for 2 h in a glass Petri dish and then the pH was measured by bringing a combined glass electrode near the surface of the film for 1 min using a portable pH meter. The pH measurement was recorded as the average of three measurements.[13]

Drug content uniformity

The drug content of selected films was determined by dissolving the films in 100 ml phosphate buffer solutions of pH 7.4 by homogenization of each film for 4 h using ultra-speed homogenizer and left to stand for 24 h with occasional shaking. Aliquots of 5 ml were withdrawn and diluted with phosphate buffer pH 7.4 to the volume of 20 ml, and the resulting solutions were filtered using 0.45 mm Whatman filter papers. The drug content was then determined spectrophotometrically at 221 nm against a blank solution of dissolved Chitosan films.[8]

In vitro muco-adhesion test

An albino rabbit weighing about 2 Kg was sacrificed. The stomach was selected as a model membrane since the stomach provided a flat and uniform surface. About 2 cm long and 0.5 cm width piece of stomach mucosa was cut and cleaned with a saline solution and then mounted on the platform of the tension-compression stand on the tensiometer. The selected film was mounted, using Scotch tape, onto the bottom face of a stainless steel disk attached to the force gauge. The piece of stomach mucosa was stapled to a piece of Scotch tape which was stuck to the bottom of a glass Petri dish, and the mucosal surface was hydrated by placing phosphate buffer pH 7.4 solution on the tissue surface. The film and the mucosal surfaces were brought into contact for 5 min. The film was then, slowly, pulled off the tissue surface following the application of force, using the knob of the instrument scale. The tensile strength required to detach the bioadhesive film from the mucosal surface was applied as a measure of the bioadhesion performance. The value for the force of detachment was measured in Mn/m by lowering the platform of the tensiometer compression stand.

Folding endurance study

Folding endurance of the films was determined by repeatedly folding one film at the same place till it broke or folded for at least 300 times manually, which is considered satisfactory to reveal good film elasticity and strength. The number of times at which the film could be folded at the same place without breaking gave the value of the folding endurance.[14]

Effect of film thickness on the drug release profile

Series of films (formulations L17-L19) of different thicknesses were prepared by the same procedure previously described.

Mathematical models

There are different mathematical models used to determine the kinetics of drug release from drug delivery systems such as zero order, first order, and Higuchi matrix controlled models.[11,12]

Zero order model

The system which releases the same amount of drug by the unit of time can be represented by the following equation:

$$Qt = Q_0 + K_{0t} \quad \text{Equation 2}$$

Where, Qt is the amount of drug dissolved in time t, Q_0 is the initial amount of drug in the solution and K_0 is the zero-order release constant.

First order model

Linear kinetics is a process that is directly proportional to the drug concentration. The release of the drug which follows first-order kinetics can be expressed by the equation:

$$Ln(100- Q) = ln(Q_0) - K_1 t \quad \text{Equation 3}$$

Where, (Q) is the percent of drug released at the time (t), (Q_0) is the initial amount of drug in the solution and (K_1) is the first-order release constant.

Higuchi model

This is the first mathematical model that describes drug release from a matrix system, proposed by Higuchi in 1963.[12] This model is based on plotting the amount or percentage of drug released from a planar system as a function of the square root of time which is described by equation 4:

$$f\,t = Q = K_H\sqrt{t} \qquad \text{Equation 4}$$

Where, K_H is the Higuchi dissolution constant, Q = Percentage or amount of drug released at time (t).

The time required for the release of half of the amount of the drug present in the film, the product half-life ($t_{\frac{1}{2}}$), was shown to be related to the film thickness by the following relationship:

$$t_{\frac{1}{2}} = \left(\frac{Ah}{2k}\right)^2 \qquad \text{Equation 5}$$

Where, A is the initial amount of the drug in the film, h: Film thickness, k: Release rate constant (Higuchi).

The $t_{\frac{1}{2}}$ values calculated by the first-order relationship:

$$t_{\frac{1}{2}} = \frac{0.693}{k} \qquad \text{Equation 6}$$

Where, k: First-order rate constant.

Statistical analysis

SPSS statistics software package (version 20) (IBM, Chicago, ill, USA) was used for logical batched and nonbatched statistical analysis. The test of significance and lack of significance among treatments at 95% confidence interval and equal to 0.05 was carried out using analysis of variance test. Tukey's allowable difference was calculated to find out the difference between treatments.

Results

In vitro drug release studies

Figure 1, shows drug release against time for films of systems I to III (films L1 to L10). Figure 2, shows drug release against time for films of systems IV to VI (films L11 to L19).

Ibuprofen release was found to be affected by the type of solvent used in the preparation of Chitosan films, the best results were obtained using 1% lactic acid as solvent in clear contrast to the use of 1% acetic acid as acidic solvent. Figures 1 and 2 depict the effect of Chitosan alone and its combination with different polymers, on the release of Ibuprofen from formulations L1 to L19. The effect of the addition of each polymer is clear and the statistical differences are shown in Table 3 which will be discussed in detail in the discussion part.

Physiochemical characterization of selected film formulations

Film surface pH study

Table 4 shows that the pH of the surface environment of selected films is ranging from 6 ± 0.057 to 6.6 ± 0.100 within the tolerance of the mucus membranes which tolerates from pH 5.6 up to pH 7.4.

Drug content uniformity

The drug content uniformity values were found to be between 96.30% and 100% of the theoretical values. The observed results of content uniformity indicated that the drug was uniformly distributed throughout all films.

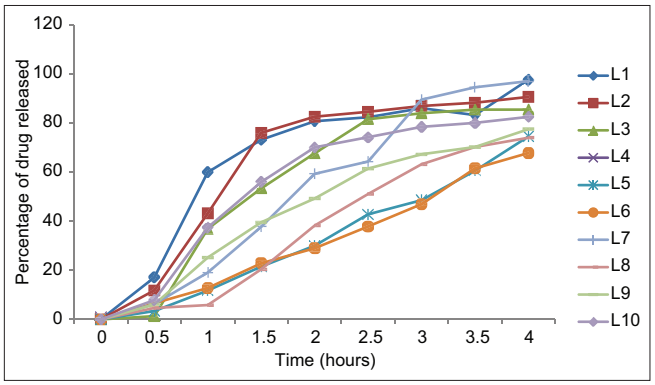

Figure 1: Percentage of Ibuprofen released from films of formulations L1–L10

Table 3: Statistical analysis of data after release studies out of selected thin films

Test	L2	L3	L4	ANOVA (*P*)	Tukey's test
Ibuprofen release after 4 h (%)	81.3	85.4	90.7	<0.05	L2 and L3 (*P*=0.041<0.05)
				0.038	L2 and L4 (*P*=0.018<0.05)
					L3 and L4 (*P*=0.305>0.05)
	74.58	67.80	97.13	<0.05	L5 and L6 (*P*=0.04<0.05)
				0.001	L5 and L7 (*P*=0.001<0.05)
					L6 and L7 (*P*=0.001<0.05)
	74.06	77.52	82.56	<0.05	L8 and L9 (*P*>0.05)
				0.045	L8 and L10 (*P*=0.025<0.05)
					L9 and L10 (*P*=0.039<0.05)
	86.40	85.60	74.72	<0.05	L11 and L12 (*P*=0.646>0.05)
				0.009	L11 and L13 (*P*=0.005<0.05)
					L12 and L13 (*P*=0.006<0.05)
	92.48	94.02	105.0	>0.05	No significant change
				0.124	
	97.76	97.12	90.56	<0.05	L17 and L18 (*P*=0.632>0.05)
				0.019	L17 and L19 (*P*=0.014<0.05)
					L18 and L19 (*P*=0.011<0.05)

Table 4: Surface pH and mucoadhesion of formulations L1, L5-L7, L14-L16, and L17-L19

Formulations	Surface pH±SD*	Force of detachment Mn/m±SD*	Formulations	Surface pH±SD*	Force of detachment Mn/m±SD*
L1	6.4±0.057	74.66±5.0332	L6	6.0±0.173	67.66±4.132
L17	6.2±0.115	71.00±2.453	L7	6.2±0.256	66.33±2.588
L18	6.0±0.057	64.00±2.338	L14	6.0±0.077	66.33±3.214
L19	6.6±0.100	63.66±3.130	L15	6.4±0.404	60.66±1.527
L5	5.9±0.001	72.33±3.511	L16	6.6±0.057	60.00±1.290

*Average of three measurements. SD: Standard deviation

Effect of film thickness on release study

Series of films of formulation L19 of different thicknesses were investigated for drug release. Table 5 shows the treatment of data after the drug release studies from films of different thicknesses using different mechanisms of drug release. Table 6 shows the treatment of data for Ibuprofen release from all studied films using different mechanisms of drug release. The significance of these results are discussed in the following discussion.

Table 5: First-order and Higuchi treatment of data for Ibuprofen release from film L19 as a function of film thickness

Film thickness	K (mg/cm² min ½) Higuchi	t½ (min)	K (min^{-1} first order)	t½ (min)
71 um±	0.067	6,854,0481.77	-0.194	3.572
84 um±	0.065	157,784,518.4	-0.320	2.165
124 um±	0.062	771,172,900	-0.706	0.981

Discussion

The percentage of drugs released from Chitosan lactic acid films was noticed to be increasing from 17% for the first half an hour and was then jumped to reach 80% after 2 h. This result is consistent with the results reported by Gorle *et al*.[15]

After 4 h of release studies, it can be clearly noticed that the percentage of drug released has significantly increased ($P < 0.05$) up to 90% as the percentage of sodium alginate has been increased in the formulations from 20% to 60% compared to the films of Chitosan alone (L1) where the drug release was quite fast (more than 80% of the drug was released in 2 h). This finding was found to be in good agreement with a work published earlier which concluded that Chitosan has limited capacity for controlling drug release when used alone.[16]

System II (L5-L7)

Figure 1 reveals that when drug loading was 20% (w/w) in each film, it is noticeable that the percentage of drugs released was the highest when the ratio Chitosan to PVP was 1:3 as the percentage of drug release reach to 97% within 4 h (formulation L7). The percentage of drug released has significantly increased ($P < 0.05$) linearly with increasing the concentration of PVP in formulations L5 to L7 which could be related to its high rate and extent of swelling. The poor aqueous solubility of the cationic polymer Chitosan has limited the swelling of the films, therefore, the addition of the hydrophilic polymer PVP is expected to increase the surface wettability and consequently water penetration within the matrix. Similar results have been reported in previous work which studied the effect of PVP on the release behavior of propranolol hydrochloride from buccal batches. This work reported that high swelling index was also exhibited by batches contain high percentage of PVP, indicating that the increase in water-soluble polymer PVP content results in faster swelling and consequently drug release from patches.[17]

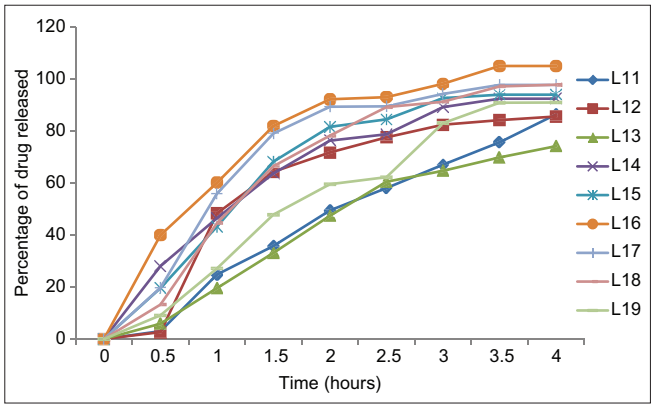

Figure 2: Percentage of Ibuprofen released from films of formulations L11–L19

System III (L8-L10)

The lower critical solution temperature (LCST) of MC is between 40°C and 50°C. MC is freely soluble in water below LCST which is 37°C in our experimental setting. Figure 1, suggests that the presence of MC in these formulations played an important role in the release of the drug from these films. Formulations L8 and L9 have shown the lower percentage of drug released 74% and 77% respectively when compared with formulation L10 with 82% drug release, when the ratio of MC to Chitosan was increased, there was a significant increase ($P < 0.05$) in the percentage of drug released which might be related to the amphiphilic and water-solubility properties of MC that is responsible for the formation of pores and channels in the matrix system, hence as expected it has lead to the increase of diffusion of the drug to the release medium.[18]

System IV (L11-L13)

As it is well known that HEC is readily soluble in cold as well as hot water. The release results of formulations composed

Table 6: Zero-order, first-order and Higuchi treatment of data for Ibuprofen release from all studied films

Films	Zero-order (K^0)	Zero-order (R^2)	First-order (K^1)	First-order (R^2)	Higuchi-model (K^H)	Higuchi-model (R^2)
L1	0.361	0.783	−0.012	0.796	0.057	0.911
L5	0.313	0.987	−0.005	0.931	0.063	0.850
L6	0.288	0.989	−0.005	0.949	0.059	0.867
L7	0.456	0.972	−0.017	0.917	0.095	0.889
L14	0.349	0.838	−0.010	0.801	0.054	0.957
L15	0.389	0.846	−0.013	0.963	0.059	0.939
L16	0.377	0.792	−0.022	0.978	0.061	0.955
L17	0.384	0.779	−0.019	0.978	0.045	0.912
L18	0.409	0.858	−0.012	0.952	0.046	0.932
L19	0.407	0.964	−0.011	0.951	0.065	0.930

of 20, 40, and 60% HEC are shown in Figure 2, which shows the percentage of drug released from the formulations L11, L12 and L13 was 86%, 85%, and 74%, respectively. The significantly lower release profile of Ibuprofen from formulation L13 (60% of HEC, $P < 0.05$) can be explained in terms of the viscosity of the polymeric solution formed once the films have been exposed to the dissolution medium. As the viscosity is related to the strength and durability of the gel layer that formed after the contact of the films with the dissolution medium. Therefore, the diffusion of the drug is expected to be low in the case of L13 films which is probably related to the viscosity of the gel layer. In addition, the relatively high swelling index of HEC increased the gel layer thickness and consequently the diffusion path length, which in turn may be the cause of the slower drug release.[19]

System V (L14-L16)

Three polymeric ratios of 3:1, 1:1, and 1:3 of Chitosan to EC are used in this system. From Figure 2, it is obvious to conclude that by increasing the ratio of EC in these formulations (L14, L15, and L16), the percentage of Ibuprofen released was noticed to jump to 60% within 1 h, knowing that there was no significant difference ($P > 0.05$) among the percentage of drug released from these formulations. This latest observation could be related to the hydrophilic/lipophilic properties of EC. Several authors pointed out that the reason might be that EC's large hydrophobic molecules could impose a discontinuity in the gel-structure leading to the formation of a weak barrier and consequently resulting in higher release rate.[20]

System VI (L17-L19)

Figure 2 depicts the data of the percentage of drug released from formulation L17 to L19. It seems that by increasing the concentration of HPC in the film formulation a corresponding significant decrease ($P < 0.05$) in the percentage of the drug released was noticed, which is probably attributed to the fact that HPC forms a strong viscous gel on contact with aqueous media, which leads to the slow release of poorly soluble drugs, in particular. Usually, water-soluble drugs are released primarily by the diffusion of dissolved drug molecules across the gel layer. The extent of polymer swelling and the hydration of the microstructure formed within the gel layer vary with the degree of polymer interaction with hydrating media.[21]

By reviewing Table 4 it is noticeable that the detachment force of all selected formulations was ranging from 60.66-74.66 Mn/m. The highest bioadhesive and bond-forming capacity with mucin was recorded for formulation L1 that contains 80% Chitosan. The film surface pH values indicate that the surface pH of these films, when swollen, will not irritate the mucus membrane on which the film will be applied**.** At neutral pH, cationic polymers such as Chitosan has numerous amine and hydroxyl groups as well as a number of amino groups that may increase the electrostatic interaction of Chitosan with the negatively charged mucin present in the rabbit stomach mucosal tissue. Slight decrease in the applied force was seen in the formulation L5 that composed mainly from 60% Chitosan and 20% PVP which may be attributed to the decrease of the percentage of Chitosan, however, by increasing the concentration of PVP and decreasing the concentration of Chitosan, a significant decrease ($P < 0.05$) in the bioadhesion force was noticed in formulations L5, L6 and L7. Very close results was reported in the literature in studies using Chitosan and PVP for the development of mucoadhesive buccal patches for Repaglinid[22] and Floxatin Hcl.[23]

Films of formulation L18 composed of equal percentage HPC and Chitosan showed a slightly higher force of attachment to the rabbit stomach compared to films of formulation L19 which are composed of the higher percentage of HPC. Very close results have been reported using Chitosan, MC, HPC, and EC for the preparation of the Naproxen buccal batch.[24] The lowest forces were recorded for formulations L14, L15 and L16 that mainly attributed to the hydrophobic properties of EC.

According to Higuchi 's diffusion-controlled mechanism of drug release, the release rate constant K has the dimension of weight per area per square root of time and should be independent of film thickness. The approximate constancy of k with varied film thickness is shown in Table 5. It was reported (26 and 27) that film thickness does affect the duration of drug release.

By reviewing Table 6 it is clear that Higuchi's release rate constant (K) is independent of film thickness (no significant change ($P > 0.05$), while the first-order release constant (k) is decreasing by the increase of film thickness. The same data

show that there is a direct relationship between film thickness and product half-life $t_{\frac{1}{2}}$ *(min)*.

Conclusion

Thin, isolatable, transparent, and elastic films of these copolymers were prepared using the solvent casting technique. Lactic acid was used as a solvent with great success compared to acetic acid. The percentage of HPC of 20% (w/w) in these selected films was found to show a higher tendency to adhere to the used mucosa making films of formulation (L17) the most ideal formulation which combines both appreciable amount of drug released (about 98% in 4 h) and high tendency to adhere to the rabbit mucosa (71.00 Mn/m) giving enough time for the drug to relieve mouth lesions and pain. The mechanism of drug release was found to follow Higuchi's diffusion model for some systems and the classical first-order kinetics for others as relatively high correlation coefficients were observed with both mechanisms compared to those of the zero-order mechanism [Tables 5 and 6].[25-27]

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Nil.

Conflicts of interest

There are no conflicts of interest.

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ملخص المقال باللغة العربية

استخدام الشيتوزان في تحضير الأغشية اللاصقة الحيوية: الغشاء القادر على تكوين واستدامة إطلاق الإيبوبروفين

المؤلفون

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الهدف: تم إدخال بوليمرات مختلفة في أغشية الشيتوزان اللاصقة الحيوية لتحقيق نجاح كبير في الحفاظ على إطلاق الإيبوبروفين لساعات قليلة، مع قوة تحمل حيوية معقولة.

التصميم: تم تحضير أغشية رقيقة وقابلة للعزل وشفافة ومرنة من هذه البوليمرات. تم تصنيف تسعة عشر تركيبة على أنها ستة أنظمة وفقًا لنسب الغروانيات المائية المستخدمة.

المواد والطرق: تم تحضير الأغشية بتقنية الصب بالمذيب. أجريت دراسة الالتصاق الحيوي باستخدام الغشاء المخاطي لمعدة أرنب ألبينو. تم استخدام المواد الغروانية المائية مثل هيدروكسي بروبيل سيولوز،والشيتوزان، والمثيل سليولوز، بالإضافة إلى البوليمرات الأخرى بالإضافة إلى الإيبوبروفين كدواء نموذجي.

النتائج: تم تأكيد القوة الميكانيكية والمرونة للأغشية مع عدم وجود علامات على الانهيار. تم العثور على الأفلام المختارة المكونة من حوالي 60٪ (وزن/وزن) هيدروكسي بروبيل سيولوز لإظهار ميل أعلى للالتصاق بالغشاء المخاطي للمعدة من النسب المئوية الأقل من نفس البوليمر. أطلقت أفلام الشيتوزان أكثر من 78٪ من محتوى الإيبوبروفين في الساعة الأولى من دراسة الإطلاق. أدى إدخال مثيل سليلوز في هذه الأفلام إلى زيادة بطيئة ولكن مستمرة في نسبة الأدوية التي تم إطلاقها، حيث وصلت إلى ذروتها بنسبة 82 ٪ بعد 4 ساعات.

الخلاصة: تم العثور على الأغشية المصنوعة من تركيبة (L17) لتكون الأكثر مثالية لكل من إطلاق كمية ملحوظة من الدواء (حوالي 98٪ في 4 ساعات) ، وميلها العالي إلى الالتصاق بالغشاء المخاطي للأرنب (71.00 مليون / م) مما يعطي ما يكفي من الوقت لممارسة تأثير الدواء محليا. تم العثور على آلية إطلاق الدواء لتتبع نموذج انتشار هيجوتشي لبعض الأنظمة والحركية الكلاسيكية من الدرجة الأولى للأنظمة الأخرى.

الكلمات المفتاحية: الأغشية اللاصقة الحيوية ، مشتقات السليلوز ، الشيتوزان ، الإيبوبروفين ، آلية إطلاق الدواء.